DISSERTATION ON

A STUDY ON
THE CARDIOVASCULAR MANIFESTATIONS
OF
SYSTEMIC LUPUS ERYTHEMATOSUS

Submitted in partial fulfilment of

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CERTIFICATE

This is to certify that this dissertation entitled **"A STUDY ON THE CARDIOVASCULAR MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS"** submitted by **Dr. SHIVA KUMAR D** appearing for Part II M.D. Branch I General Medicine Degree examination in September 2006 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I solemnly declare that the dissertation titled "A STUDY ON THE CARDIOVASCULAR MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS" is done by me at Madras Medical College & Govt. General Hospital, Chennai during 2004-2005 under the guidance and supervision of Prof. V.K. Rajamani, M.D.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with worldwide distribution and affects all races. It is more common in blacks and females, particularly of childbearing age.

The sex distribution is 1:8 (♂ : ♀) in adults. It is a systemic disease with varied manifestations. It is diagnosed by the following criteria.

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Non-erosive arthritis of two or more peripheral joints
6. Serositis
7. Renal disorder – Proteinuria > 0.5 g/day or cellular casts
8. Seizures or psychosis without other causes
9. Hemolytic anemia or leucopenia or lymphopenia or thrombocytopenia in the absence of offending drugs

10. Presence of Anti-dsDNA, anti-Sm, and / or anti-phospholipid antibodies
11. An abnormal titer of ANA by immunofluorescence or an equivalent assay at any point in time in the absence of drugs known to induce ANAs.

When 4 criteria are fulfilled, it is diagnostic of SLE. It's a systemic disease with significant morbidity. The manifestations are varied and differ from time to time. They change because of the disease activity itself or due to treatment.

Cardiac involvement in SLE in relatively common. It may be transient or permanent. Pathologically, the pericardium, myocardium, endocardium and the coronary arteries may be involved.

The patients with cardiac involvement are mostly asymptomatic. When symptomatic, they may have chest pain attributable to pericarditis. Anginal pain can occur at any age in SLE patient because of accelerated atherosclerosis due to long term steroid therapy or rarely due to coronary arteritis.

Symptoms of congestive cardiac failure due to myocardial dysfunction or valvular disease include shortness of breath, pedal edema and fatigue. These can occur also due to anemia, renal and pulmonary involvement.

Syncopal attacks due to conduction disturbances in SLE are quite rare.

The symptoms subside or abate with steroid therapy proving the immunological basis of the cardiovascular involvement.

Since many patients are asymptomatic, a thorough examination of the cardiovascular system by ECG, CXR and ECHO reveals hitherto silent pericarditis, valvular heart disease or myocardial dysfunction.

AIMS AND OBJECTIVES

- To study the various cardiac manifestations in SLE
- To know the incidence of cardiac involvement in SLE in the study group
- To know the common cardiac manifestations in the study group

REVIEW OF LITERATURE

Cardiac abnormalities are one of the most important clinical manifestations of **Systemic Lupus Erythematosus** (SLE), contributing significantly to the morbidity and mortality of this disease. Including arterial hypertension, cardiac involvement has been reported in from 52 to 89% of patients *(1-5)*. The pathologic picture is that of a pancarditis affecting the pericardium, myocardium, endocardium and coronary arteries. Involvement of one layer of the heart, such as a pericarditis, may dominate the clinical picture in one patient, whereas in another, the heart may be diffusely affected.

At times, it is difficult to differentiate between primary cardiac charges resulting from SLE and those resulting from complicating conditions. Frequently occurring symptoms that are referable to the heart and the cardiovascular system must be carefully evaluated and differentiated from non cardiac symptoms, which they can mimic. Symptoms of angina pectoris, hypertension, cardiac failure and pericarditis frequently mimic those of esophageal spasm, reflux esophagitis, pleurisy, pneumonitis, and costochondritis. The prevalence of

cardiovascular abnormalities in SLE has been based mostly on retrospective material or on highly selective series of patients. A prospective study of cardiovascular disease in all adult patients with lupus living within a defined area in southern Sweden over a mean period of 5.6 years was completed *(6)*. A high frequency of pericarditis (35%), valvular heart disease (27%), mild pulmonary hypertension (16%), and decreased left ventricular function (19%) was found. Ischemic heart disease was observed in 17%.

PERICARDITIS

Pericarditis is diagnosed in proportion to the care of the examination.

Involvement of the pericardium in SLE, which was first recognized by ***Keefer and Felty*** *(7)* in 1924, is a common feature, and it is the most common cardiac abnormality in this disease. In several reported series, the prevalence of pericarditis has ranged from 6 to 45%. ***Godeau et al.*** *(8)* diagnosed pericarditis in 27% of 112 patients, and ***Rothfield*** *(9)* diagnosed pericarditis in 25% of more than 200 patients.

Doherty and Seigel *(10)* found the prevalence of pericarditis to be 25.6% among 1194 patients with SLE who were collected from several clinical series in the literature. In contrast, they found a prevalence of 62.1% among 254 autopsy cases, indicating that asymptomatic pericardial involvement is common. Moreover, the diagnosis may be missed unless the patient is specifically questioned about its clinical manifestations. Introduction of echocardiography as a diagnostic modality has confirmed the high frequency of asymptomatic pericardial effusion and thickening in patients with SLE.

Acute pericarditis may occur as an isolated finding or as part of a generalized serositis. ***Estes and Christian*** *(11)* noted cardiac manifestations in 38% of their 150 patients. Pericarditis occurred in 29 patients and was associated with pleural effusions in all but 7.

The clinical picture of lupus pericarditis usually is typical, with complaints of substernal or pericardial pain aggravated by motion such as breathing, coughing, swallowing, twisting and bending forward. At times, a pericardial rub may be heard in an

asymptomatic patient. Symptoms may be severe and persistent or mild and transitory. Complaints may last for hours or weeks, and they often recur over a period of years. Pericarditis usually develops during the subacute or chronic period.

M-mode and two dimensional (2-D) echocardiography are the current methods of choice for diagnosing pericardial effusions. ***Ito et al.*** *(12)* found effusions in 46% of 48 selected patients with SLE undergoing echocardiography. ***Bomaski et al.*** *(13)* noted effusions in 49% of 47 patients, and ***Chia et al.*** *(14)* described effusions in 24% of 21 unselected patients. Using both M-mode and 2-D echocardiography, ***Doherty et al.*** *(15)* found pericardial effusion in 42% of 50 patients with SLE who were studied retrospectively.

Recent studies have compared the echocardiographic findings in unselected patients with SLE with those in age and sex-matched healthy controls. ***Klinkoff et al.*** *(16)* found pericardial involvement in 10 of 47 patients with SLE (21%) and in none of 46 healthy controls. Effusion was present in 4 patients and pericardial thickening in 6. ***Crozier et al.*** *(17)* found pericardial effusion in 27 of 50 Chinese patients with SLE

and in 5 of 50 matched controls, with the significantly larger effusions in the patients with SLE. ***Cervera et al.*** *(18)* found effusion in 19 of 70 patients with lupus (27%) and in none of 40 matched controls. Five patients (7%) with severe to moderates effusions had clinical and ECG features of pericarditis. In contrast, 14 patients (20%) with small effusions did not have clinical pericarditis.

Cardiac Tamponade

Despite the high frequency of pericarditis and effusion, cardiac tamponade rarely occurs in SLE. It may develop at any point during the course of the disease, however, and should be considered in patients with signs of venous congestion.

Of 150 patients with SLE who were followed prospectively by ***Estes and Christian*** *(11)*, 29 developed pericariditis, and only 2 of these developed cardiac tamponade that required pericardial fenestration. The prevalence of cardiac tamponade was 0.8% in a combined series of 15 studies consisting of 1332 patients with SLE *(10)*. A retrospective study of 75 patients with lupus and pericarditis *(19)* found 11 episodes of cardiac

tamponade in 10 patients (13%). Tamponade was the presenting manifestation of SLE in 4 patients, and the remaining 7 episodes occurred during the active phase of the disease. Tamponade was fatal in one patient. Cardiac tamponade has been reported as the initial manifestation of the disease in a few pediatric and adult cases, as well as in late-onset SLE .

Constrictive Pericarditis

Constrictive pericarditis results from chronic fibrous thickening of the wall of the pericardial sac, causing impairment of normal diastolic filling of the heart . Only very few cases of constrictive pericarditis resulting from SLE have been described *(20)*. All reported cases, except one, were males. Male predominance also is observed in constrictive pericarditis resulting from other causes . The condition developed while patients with lupus on systemic corticosteroids, and pathologic findings included hyalinized fibrotic thickening of the pericardium and perivascular mononuclear infiltrates . Constrictive pericarditis also has been seen in patients with

drug-induced LE resulting from procainamide and from hydralazine *(21)*.

MYOCARDITIS

Primary myocardial involvement in SLE is uncommon.

Myocarditis was diagnosed clinically in 8% of 520 patients by ***Dubois*** *(22)*, in 8% of 150 patients by ***Estes and Christian*** *(13)*, and in 10% of 128 patients by Ropes *(23)*. ***Borenstein et al.*** *(24)* found 5 cases of myocarditis in 140 patients with SLE who were reviewed retrospectively for myocardial disease. In a prospective study of 100 patients with SLE for cardiovascular manifestations, myocarditis was diagnosed in 14% *(25)*.

The clinical picture of SLE myocarditis is similar to that of myocarditis resulting from viral infection or some other cause. The earliest change usually is tachycardia, which is disproportional to the fever. The heart becomes diffusely enlarged, often with the point of maximal impulse at the anterior axillary line. The patient may have dyspnea, palpitations, heart murmurs, sinus tachycardia, ventricular

arrhythmias, gallop rhythm, and/or congestive heart failure. The diagnosis of SLE myocarditis often is difficult to make clinically, because other factors that can lead to congestive heart failure such as anemia, uncontrolled hypertension, systemic infection, valvular disease, or fluid and salt retention resulting from renal disease or systemic corticosteroid use, also may be present.

At autopsy, SLE myocarditis is diagnosed more frequently than is reported in clinical series. Among 236 autopsied SLE cases that were collected by ***Doherty and Siegel*** *(10)* from eight separate reports, myocarditis was found in 100 (40%). The pathological abnormalities vary in severity, usually consisting of small foci of interstitial plasma cell and lymphocyte infiltrates and, rarely, of a widespread, diffuse, interstitial inflammation, fibrinoid change and hematoxylin bodies are seen. Small foci of patchy myocardial fibrosis are common in corticosteroid-treated patients.

MYOCARDIAL FUNCTION ABNORMALITIES AND CONGESTIVE HEART FAILURE

Myocardial function abnormalities are frequently found in patients with SLE, even in those without cardiac symptoms.

Strauer et al. *(26)* studied cardiac hemodynamics during right and left-heart catheterization in five young, female patients with SLE and without clinical symptoms and signs of cardiac disease. Evidence of impaired pump function, reduced contractility, increased myocardial wall stiffness, and decreased coronary artery reserves were found. It was suggested that lupus cardiomyopathy may affect intrinsic contractile properties of the myocardium and frequently may occur subclinically.

Del Rio et al. *(27)* compared systolic time intervals, a noninvasive method that is helpful in assessing myocardial function, in 25 patients with SLE and 22 healthy controls. The patients had shorter left ventricular ejection times and longer pre-ejection periods than the controls, suggesting impaired left ventricular systolic function. These abnormalities were independent of age, duration of SLE, blood pressure, anemia, renal disease, steroid treatment and immunologic activity.

Crozier et al. *(17)* reported that compared to healthy controls, patients with SLE have significantly decreased left ventricular ejection fractions and diastolic compliance and increased left ventricular systolic dimensions. These abnormalities were not explained on the basis of hypertension or coronary artery disease, suggesting primary myocardial involvement.

Studying a group of patients with lupus and stable disease, ***Enomoto et al***. *(28)* found normal left ventricular systolic functions but decreased left ventricular diastolic function, which appeared to worsen progressively with age. Diastolic dysfunction can result from hypertension, steroid therapy, or primary myocardial involvement by SLE. However, the presence of diastolic dysfunction in young normotensive patients with lupus on a short duration of steroid therapy suggest that the latter mechanism is responsible for the myocardial abnormality.

Newer techniques, including radionuclide ventriculography confirms the high prevalence of left ventricular dysfunction in SLE. The abnormalities are subclinical, however, and whether

these are clinically significant over time has not been fully investigated in prospective studies. Recently, ***Winslow et al.*** *(29)* reported abnormalities in systolic and diastolic left ventricular function to be progressive over time, leading to a decline in ventricular function and an increase in left ventricular mass and size. In contrast to the findings of other investigators, they found that these abnormalities were related to hypertension and coronary artery heart disease. In normotensive patients with lupus, mild functional abnormalities *(Presumably resulting from SLE)* did not worsen during a 5 year observation period. This important study suggests that primary involvement of the myocardium in SLE does not commonly *(by itself)* lead to clinically significant changes in left ventricular size and function, and that other pathogenetic factors, especially hypertension and atherosclerosis, are more important.

Decreased left ventricular function was noted by ***Sturfelt et al.*** *(6)* in 14 of 75 patients with lupus (19%) who were followed prospectively. Five had myocardial infarction, and in the remaining 9, who had no clinical evidence of myocardial infarction, left ventricular dysfunction was mild. Thus, this study

confirms that severe global left ventricular hypokinesia is not a common feature of SLE.

Effect of treatment on Myocardial Function

Myocardial function in a group of patients with SLE and active disease was assessed before the initiation of corticosteroid therapy and when the illness became inactive following steroid therapy. Using computer-assisted analysis of digitized echocardiograms, ***Murai et al.*** *(30)* found evidence of left ventricular systolic and diastolic dysfunction that reversed with treatment.

Thus the data from various noninvasive studies consistently indicate that abnormalities in myocardial function are common in patients with SLE and active disease, even in the absence of overt cardiac symptoms. That these abnormalities reverse with steroid therapy supports an immunologic basis for the myocardial dysfunction.

Congestive Heart Failure

The clinical diagnosis of congestive heart failure in SLE is often difficult, because manifestations of activity of the underlying disease can mimic the symptoms of cardiac failure. Failure often is preceded by fever, tachycardia, hepatomegaly, and hypertension associated with nephropathy. Corticosteroid therapy can aggravate these processes. Dyspnea resulting from pleuritis, ascites, or primary diaphragmatic dysfunction, other factors that may contribute or aggravate congestive heart failure, such as valvulitis, myocarditis, pericarditis with effusion, and anemia, often are present. Because they may coexist, it often is difficult to ascertain how much of the patient's dyspnea and other symptoms result from cardiac decompensation and how much result from other manifestations of the disease.

Congestive heart failure was diagnosed clinically in 5% of ***Dubois's*** 560 patient *(22)* and in 11% of ***Estes and Christian's*** 150 patients *(11)*. Of 100 patients with SLE who were followed prospectively by ***Badui et al.*** *(25)* for cardio vascular manifestations, 10 developed congestive heart failure. This was associated with myocarditis in 5 patients, hypertension in 4, and vascular heart disease in 1. Congestive heart failure occurred in 10 of 142 patients. (7%) reported by ***Hejtmancik***

et al. *(20)*, and myocarditis was the major cause of heart disease in 6. All 5 patients who succumbed to heart failure had pathologic evidence of myocarditis at autopsy. In contrast, ***Brigden et al.*** *(2)* diagnosed cardiac failure in 22 of 60 patients with SLE, and hypertension was the major cause. Rarely, however, was it the sole responsible factor. Decompensation with a low or normal blood pressure developed in 5 patients, 3 of whom had pericarditis and 1 of whom bacterial endocarditis. Myocarditis as the sole cause of cardiac failure was not seen in any of these patients.

ENDOCARDITIS AND VALVULAR HEART DISEASE

Libman-Sacks ***"atypical verrucous endocarditis,"*** is the most characteristic and classic cardiac lesion of SLE, comprised of verrucous vegetations that range from 1 to 10 mm in diameter. Grossly, the verrucae appear as *"granular, tawny or pinkish, pea-sized masses densely adhered to the underlying endocarduim and formed single or conglomerate and sometimes mulberry-like clusters"*. The lesions are found near the edge of the valve, on both surfaces of the valves, on the rings and commissures, and less frequently, on the chordae tendinea, papillary muscles, and atrial and ventricular mural

endocardium . The vegetations can develop in any valve and often are multivalvular. ***Libman and Sacks*** *(31)* as well as ***Gross*** *(32)* noted the verrucae most commonly in the tricuspid valve, but more recent studies have found a higher frequency on the mitral valve *(4)*, especially in the recess between the posterior valve leaflet and the ventricular wall .

The diagnosis of ***Libman-Sacks*** endocarditis can only be made with certainity at autopsy or at surgery. The prevalence of these lesions varies greatly among autopsy series ranging from 13 to 74%. Before the availability of steroids, ***Doherty and Siegel*** *(10)* found a prevalence of 59% among 86 autopsy cases reported in the literature. In contrast, 35% of 236 autopsy cases reported after 1953 who had received steroids had ***Libman-Sacks verrucuous lesions***.

Another explanation for the decreasing prevalence may be that the endocardial lesions formerly were considered to be a requisite to the diagnosis, because these constituted the most specific gross postmortem findings, whereas the diagnosis of SLE now is made primarily on clinical grounds. Thus, the latter

series would not be weighted in favour of endocardial involvement.

The clinical diagnosis of Libman-Sacks endocarditis is difficult. Physical findings and echocardiographic abnormalities may suggest the diagnosis, but they are not diagnostic. Many patients with active SLE have tachycardia, anemia and fever, all of which may be associated with a cardiac murmur. Thus, it often is difficult to interpret the significance of murmurs, even if they are of greater intensity.

Libman-Sacks endocarditis rarely produces hemodynamic changes, but it has been associated with ruptured chordae tendineae, aortic stenosis, thromboembolic disease , and cerebral emboli . Rarely, Libman-Sacks vegetation may mimic a large intracardiac tumor.

Valvular Heart Disease.

It now is recognized that hemodynamically and clinically significant valvular disease occurs in patients with SLE and may require prosthetic valve replacement. Aortic insufficiency represents the most commonly reported lesion . ***Doherty and***

Seigel *(10)* collected 36 cases in the English literature and concluded that the insufficiency probably results from multiple factors, including Libman-Sacks endocarditis, fibrinoid degeneration causing thinning and fenestration of the valve cusps, distortion of the valve tissue by fibrosis, valvulitis, bacterial endocarditis, aortitis, and aortic dissection. They identified systemic hypertension, steroid therapy, bicuspid aortic valves and rheumatic fever as risk factors in some of the patients.

Few cases of significant isolated mitral insufficiency or of combined mitral and aortic insufficiency have been described in patients with SLE. ***Bulkley and Roberts*** *(33)* have suggested that steroid therapy leads to the healing of verrucae and fibrous scarring. The posterior mitral leaflet and its chordae tendineae become shortened and adhere to the underlying mural endocardium, causing mitral regurgitation. Other causes include fibrinoid necrosis of the papillary muscles and rupture of the chordae tendineae .

Color Doppler echocardiography has shown a high frequency of valvular regurgitation in SLE, with right-sided

regurgitation being more common than left-sided regurgitation. Right-sided regurgitation may be related to pulmonary vascular lesions causing increased pulmonary artery pressure *(34)*.

Infective Endocarditis

Libman-Sacks endocarditis may be complicated by infective endocarditis. An analysis of 15 reports by ***Doherty and Siegel*** *(10)* showed that 4.9% of Libman-Sacks endocarditis cases diagnosed at autopsy and 1.3% of clinically diagnosed cases were complicated by infective endocarditis. Bacterial endocarditis was diagnosed in 6 of 571 patients with SLE who were admitted to the National Institutes of Health (NIH) and in 2 of 142 patients seen by Ropes (23). In the NIH study, all 6 patients were treated with corticosteroids, and 4 had pre-existing heart murmurs. Endocarditis occurred after dental procedures in 2 patients and for no known cause in 4. Endocarditis was diagnosed in 1% of patients with SLE, which is a greater percentage than that of any other connective tissue disease seen at the NIH. Antibiotic prophylaxis is recommended

before operative dental or other surgical procedures in all patients with SLE. The need for prophylaxis is further supported by the disproportionately high frequency of mitral valve prolapse in SLE diagnosed by echocardiography.

Coronary Artery Disease and Myocardial Infarction

The prevalence of coronary artery disease (CAD) and or myocardial infarction in patients with SLE appears to be increasing. The occurrence of myocardial infarction in female patients with lupus younger than 35 years of age has been reported *(10).*

Different mechanisms, acting either solely or in combination, are implicated in the pathogenesis of CAD and myocardial infarction in patients with SLE. Atherosclerosis, a pathologic process that is accelerated by long-term corticosteroid use, is by far the most common. Vasculitis involving the extramural coronary arteries and resulting in luminal occlusion is another such cause, although this is rare. Other mechanisms include coronary arterial spasm and acute

coronary artery obstruction from an insitu thrombus or embolus.

In an authoritative study of risk factors for CAD, ***Petri et al***. *(35)* found CAD in 19 of 229 patients with SLE (8.3%) who were studied longitudinally. They also identified independent risk factor for CAD: Older age at diagnosis of SLE, hypertension, hypercholesterolemia, duration of SLE, obesity, and duration of steroid therapy. Over a period of 3 years, CAD accounted for 30% of all deaths in their patients. More important, they found that cardiac risk factors were very prevalent in their lupus patient population, whose average age was only 38.3 years. Three or more known risk factors were identified in 53% of their patients, even in those who were not on steroid therapy during the study, yet only 17% of their patients were aware that they were at risk for developing CAD. Regression analysis showed that an increase in prednisone dose of 10 mg daily was associated with significant changes in serum cholesterol, blood pressure and body weight. They also found that hydroxychloroquine therapy was associated with lower serum cholesterol, suggesting an additional benefit from this agent.

Myocardial infarctions have been reported in patients with SLE less than 35 years of age, and even as young as 5 years . In 1982, ***Homey et al.*** *(36)* described six cases of ischemic heart disease in patients SLE aged 15 to 29 years. Of these patients, three patients had atherosclerotic lesions, and one was helped by coronary artery bypass surgery. Coronary arteritis was found in three patients; one of these was diagnosed during life and benefited from systemic corticosteroids.

ECG changes and Conduction defects

The ECG records can be useful in the diagnosis and treatment of patients with SLE. It is of particular value in equivocal cases, in whom the tracing shows changes suggestive of pericarditis or myocarditis that are not apparent by history and physical examination, thereby alerting the clinician to evaluate carefully for evidence of multisystem disease. The ECG may show abnormalities that are caused by electrolyte imbalance, which are not uncommon in patients with renal or cardiac disease who are receiving corticosteroids and /or diuretics.

Abnormal ECGs often are found in patients with SLE, but no changes actually are considered to be characteristic of the disease *(5)*. Abnormal tracings were found in 34% of 291 patients by ***Dubois*** *(22)* and in 74% of 100 female patients with SLE who were followed by ***Badui et al.*** *(25)* specifically for cardiovascular disease. Differences in patient selection, frequency of obtaining in ECG, and other factors probably account for the wide variation in the prevalence of abnormalities.

Conduction Defects

Conduction defects and rhythm disturbances are not uncommon in patients with SLE. The prevalence is not known, although it seldom has been reported to be more than 10%. Studies using constant ECG monitoring are not available. Different type of abnormalities have been described, including bundle-branch block, atrioventricular block, complete heart block, and atrial premature contraction. First-degree heart block is uncommon in patients with SLE; it is more characteristic of

acute rheumatic fever. However, occasional patients with first-degree block in SLE have been reported *(3, 4, 25)*.

Persistent Tachycardia

Estes and Christian *(13)* observed persistent sinus tachycardia in the absence of fever or other manifestations of heart disease in 19 of 150 patients. This often presents a clinical problem in management if the patient is otherwise asymptomatic.

Echocardiography and other noninvasive cardiac laboratory tests are indicated to exclude myocardial dysfunction. Increasing the dosage of steroids may suppress the tachycardia in some patients. In the absence of other evidence of cardiac disease, however, it may be necessary to use a steroid dose that partially controls the tachycardia but has no excessive side effects. β-Blockers such as propranolol may be helpful in patients with symptomatic sinus tachycardia.

Hypertension

Arterial hypertension is a common feature of SLE. Blood pressure readings of more than 140/90 mm Hg were found at some time in the clinical course in 25% of ***Dubois'*** 520 patients *(22)*. The mean prevalence of hypertension in nine published series of SLE patients is 28.8% (range, 12-49%)

Hypertension was reported to be less prevalent in patients with SLE and rheumatoid-like polyarthritis, especially in those without nephritis and in blacks . It is speculated that the "protective" effect of the polyarthiritis is conferred by a higher frequency of the DR4 allele.

Hypertension in SLE is related to the development of nephropathy and to the use of systemic corticosteroids. In 1948, ***Humphreys*** *(37)* suggested that in the absence of renal disease, the blood pressure in patients with SLE is normal or, more often, low.

Subsequent investigators have confirmed the frequent association between hypertension and renal disease in SLE.

Brigden et al. *(2)* reported that of 26 hypertensive patients with SLE in their series, 20 had renal disease, 2 had incidental essential hypertension, and the remaining 4 developed hypertension while on systemic corticosteroids. A retrospective analysis of 232 patients with SLE at the NIH revealed that hypertension occurs early during the course of SLE in many patients, and that it is not necessarily associated with clinical severe renal disease *(38)*. Two-thirds of the hypertensive patients with SLE had a creatinine clearance of more than 60 mL/min and nonnephrotic-range proteinuria. Moreover, only 60% of these patients with biopsy proven diffuse glomerulonephritis were hypertensive. Normotensive patients with SLE tended to be on a lower dosage of corticosteroids than the hypertensive patients, but considerable overlap occurred between the two groups.

Hypertension is a frequent finding in patients who are taking systemic corticosteroids for asthma, SLE, and other diseases. The hypertension probably results from several mechanisms, including fluid and sodium retention, increased sensitivity to endogenous catecholamines and increased production of *angiotensinogen.*

Long-standing hypertension can lead to the development of myocardial hypertrophy in patients with SLE. Although hypertension is a major factor in the pathogenesis of congestive heart failure in SLE, it rarely is the only cause. Other predisposing factors often are present, such as anemia, myocarditis, pericarditis, infection, and corticosteroid use.

Ginzler et al. *(39)* showed that hypertension occurring at any time during the course of SLE is a risk factor for deterioration in renal function and for renal death, and that is independent of steroid therapy and active nephritis. The high proportion of black patients, who are known to have a higher prevalence of hypertension, may have contributed to the outcome of this study.

Effect of Corticosteroids on the Heart in SLE

Long-term use of systemic corticosteroids for the treatment of SLE can result not only in an increased prevalence of hypertension, left ventricular hypertrophy, and congestive heart failure but also in other important changes in the heart.

In the steroid-treated patients, the Libman-Sacks endocardial lesions were smaller, fewer in number, and involved single rather than multiple valves. The mitral valve was most commonly involved in the steroid-treated patients and the lesions showed evidence of partial or complete healing.

The pericardium in nonsteroid-treated patients showed active fibrinous changes. In contrast, steroid-treated patients most commonly showed a fibrous (*i.e., healed*) pericarditis and, occasionally, infective pericarditis. The focal lesions of lupus myocarditis were found less frequently in the steroid-treated patients. Steroid-treated patients with SLE showed increased amounts of epicardial fat and intramyocardial fat, especially in the right ventricle, probably analogous to the deposition of subcutaneous adipose tissue in the face and upper back. Finally, steroid-treated patients showed a greater degree and frequency of narrowing of extramural coronary arteries by atherosclerotic plaques, leading to significant ischemic heart diseases.

CARDIAC ABNORMALITIES AND ANTICARDIOLIPIN ANTIBODIES

The presence of cardiac abnormalities in SLE is strongly associated with increased levels of anticardiolipin antibodies. The sensitivity and specificity of high levels of anticardiolipin antibodies in the prediction of cardiac abnormalities is 78% and 74% respectively. **Nihoyannopoulos et al (40)** demonstrated high levels of anticardiolipin antibodies in 50 cases of SLE of which 39 had had atleast one cardiac abnormality.

Chest Pain

Chest pain is a frequent complaint of patients with SLE. The evaluation of such a patient is based on the same principles that are followed for any patient presenting with acute or chronic chest pain. A thorough clinical history and careful physical examination are the cornerstones of the diagnostic process. Certain clinical entities, however, should be remembered when formulating the differential diagnosis of chest pain in SLE, because these conditions may be relatively more prevalent in these patients.

Cardiac Causes

Acute lupus pericarditis probably is the most common cause of chest pain of cardiac origin in patients with SLE. The patient may present with the typical retrosternal pain that builds in intensity; is aggravated by lying down, swallowing, and/or inspiration ; and eases with sitting and leaning forward. Concomitant pleurisy often is present. Angina pectoris should be considered, even in a young female, because long-term steroid therapy can lead to accelerated atherosclerosis and CAD. Although rare, arteritis of the extramural coronary arteries can develop, resulting in myocardial infarction. Other cardiac causes include chest pain that is associated with mitral valve prolapse, which appears to be more prevalent among patients with SLE.

Pleurisy, with or without effusion, is one of the most common intrathoracic causes of chest pain in patients with SLE. Pleurisy may not necessarily be a result of the underlying disease but of tuberculosis or other infections. Bacterial pneumonia can present with pleuritic or nonpleuritic chest pain. Pulmonary embolism should be considered in the differential diagnosis of acute chest pain, particularly in those with antiphospholipid antibody syndrome. It must be stressed that

pulmonary embolism may occur even in patients who test negative for aCL antibodies or lupus anticoagulant. Less frequent causes of chest pain include diffuse spasm and other esophageal abnormalities as well as pulmonary arterial hypertension. Patients on aspirin or other NSAIDs and corticosteroids are prone to gastritis and peptic ulcer disease, and when complicated by esophageal reflux, epigastric and retrosternal pain may develop.

Pain arising from musculoskeletal structures should be specifically sought. Costochondritis and fibromyalgia are not uncommon in patients with SLE, and both conditions are characterized by thoracic or chest wall pain *(6)*. The examiner should palpate for tender points in the upper chest, trapezius, and infrascapular regions. Osteoporosis complicating chronic steroid therapy predisposes to rib fractures and vertebral body collapse.

Renal vein thrombosis in a patient with lupus nephritis and nephritic syndrome may present with pleuritic chest pain.

In choosing the laboratory investigations that are needed to evaluate an individual patient, the clinician should be guided by the clinical history and physical findings. A chest radiograph, ECG, and echocardiogram are helpful when intrathoracic causes of chest pain are being considered. The laboratory diagnoses of acute pulmonary embolism, angina pectoris, myocardial infarction, and chronic pain associated with esophageal abnormalities are basically the same in patients with lupus as in other patients without SLE. When exacerbation of the underlying disease is suspected, serologic markers of disease activity, such as anti-dsDNA and serum complement levels should be obtained. Evidence of other organ involvement should be sought. Tests for aCL antibodies and lupus anticoagulant are helpful in those patients with thromboembolic disease and valvular heart disease.

MATERIALS AND METHODS

SLE patients(those patients who met 4 or more of the Classification Criteria for the diagnosis of SLE) in GGH – outpatient or inpatient in various wards of medicine, rheumatology and nephrology were assessed for cardiac symptoms and signs.

ECG, CXR and ECHO was performed in all these patients. HRCT was done in selective patients.

All patients were

- questioned for the symptoms of chest pain, syncope, palpitations, dyspnea

- examined for pulse, BP, intensity of S1, S2, the presence of murmurs, pericardial rub, S3

- ECG was analysed for sinus tachycardia, arrhythmias, heartblock, features of

pericarditis, hypertensive changes and Ischemic heart disease.

- CXR was analysed for cardiomegaly, pleural effusion, pulmonary hypertension, reticulonodular shadows and peripheral wedge shape capacities.

- ECHO was done to evaluate

  (1) Presence of pericardial effusion, thickening

  (2) Chamber dilatation, hypertrophy, presence of myocardial dysfunction – Systolic or diastolic

  (3) Valvular lesions

  (4) Presence of vegetations.

INCLUSION CRITERIA

Patients who met atleast 4 of the 11 classification criteria for the diagnosis of SLE were included in the study.

EXCLUSION CRITERIA

Patients with clinical features of mixed connective tissue disorders

OBSERVATION

The study group included 45 patients. There were 41 females and 4 males patients. The ratio of female to male is 10:1. The age distribution range from as low as 14 years to upto 40 years, with the majority being young adult females of reproductive age group.

Of the 45 patients, only 15 had symptoms referable to cardiovascular system, when confounding factors like fever, anemia, pleurisy, renal failure were excluded as the cause of symptoms. This amounted to 33% of total patients.

The common symptoms in decreasing order of frequency are furnished in table below:

Symptoms	Frequency
Exertional dyspnea	8
Palpitations – Paroxysmal, Regular	7
Chest Pain – More of pericarditis like pain	5
Pedal edema – in patients with congestive cardiac failure	3

Clinical examination revealed the following signs in decreasing order of frequency

Signs	Frequency
Hypertension (SBP>= 140, DBP>=90mm Hg)	6
Pericardial rub	4
Elevated JVP	4
Tachycardia	4
Bibasal fine inspiratory crepitations	4
Systolic murmur in the apex	2
Midsystolic ejection click in the Mitral Area	2
S3	1
Loud P2	1

ECG tracings were normal in 25 patients of our study. Of the remaining 20 patients, Sinus tachycardia was present in 15 patients. The other findings were

LVH	2
T inversion in inferior leads	2
Low Voltage complexes	1
Poor progression of R wave	1
Diffuse ST – T changes	1
Incomplete RBBB	1

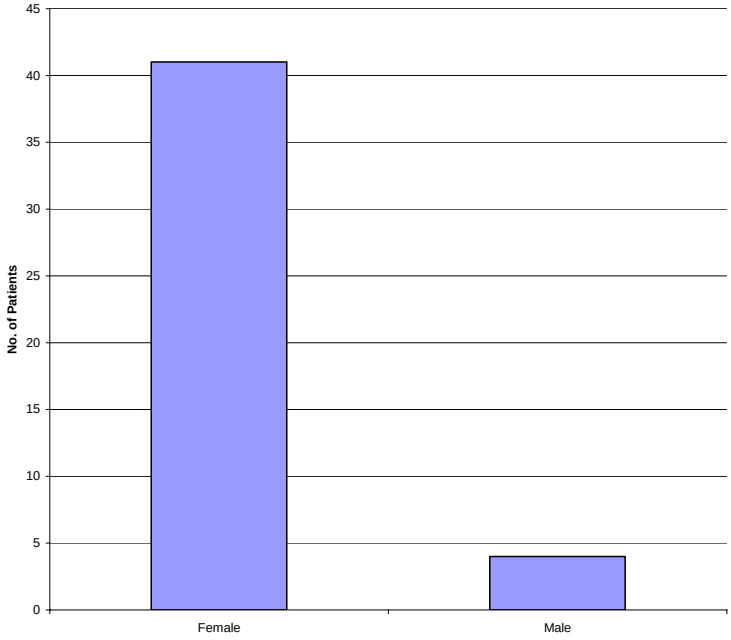
CXR revealed cardiomegaly in 7 patients, pleural effusion in 2 patients and prominent Main Pulmonary artery in 1 patient.

ECHOcardiogram was able to identify cardiac lesions in 24 of the 45 patients. The findings in decreasing order of occurrence are

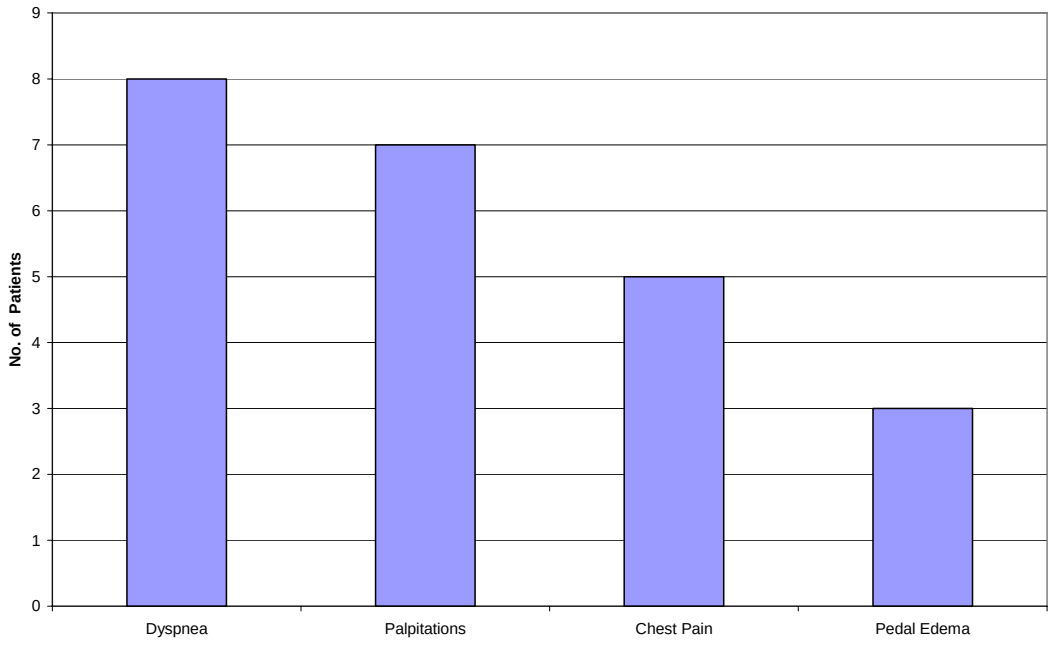
Pericardial effusion	12
MVP	11
MR	8
LVH	3
AR	2
Global Hypokinesia	2
Regional hypokinesia	1
TVP	1
TR	1
Diastolic dysfunction	1
PHT (moderate)	1

Of the total 45 patients, 24 had evidence of cardiovascular involvement.

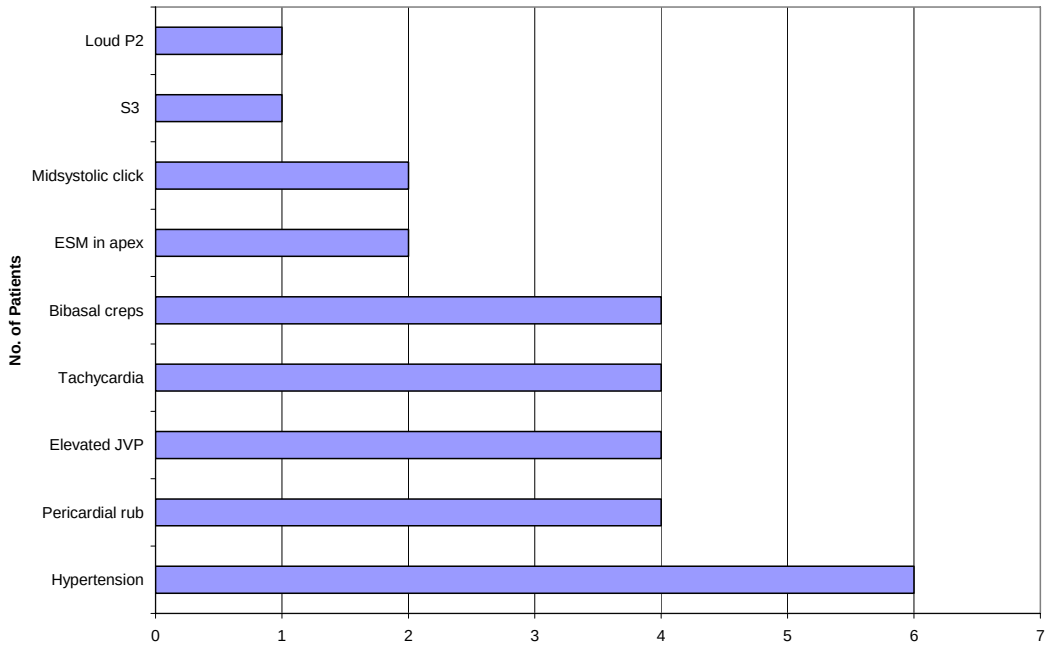
Sex distribution in the Study Group



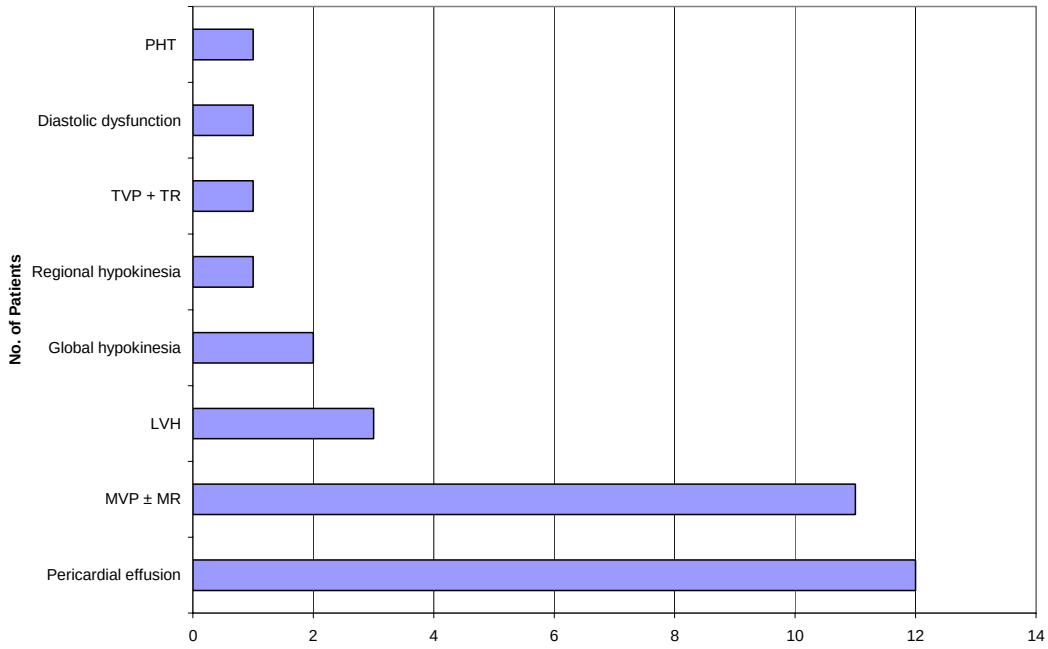
Cardiac symptoms



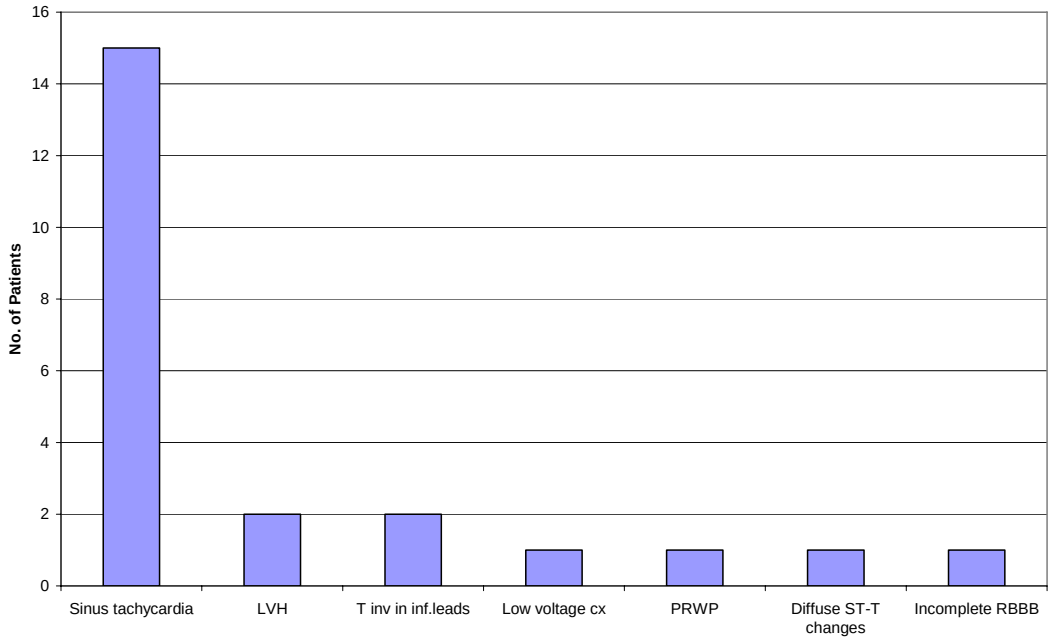
Cardiac Signs



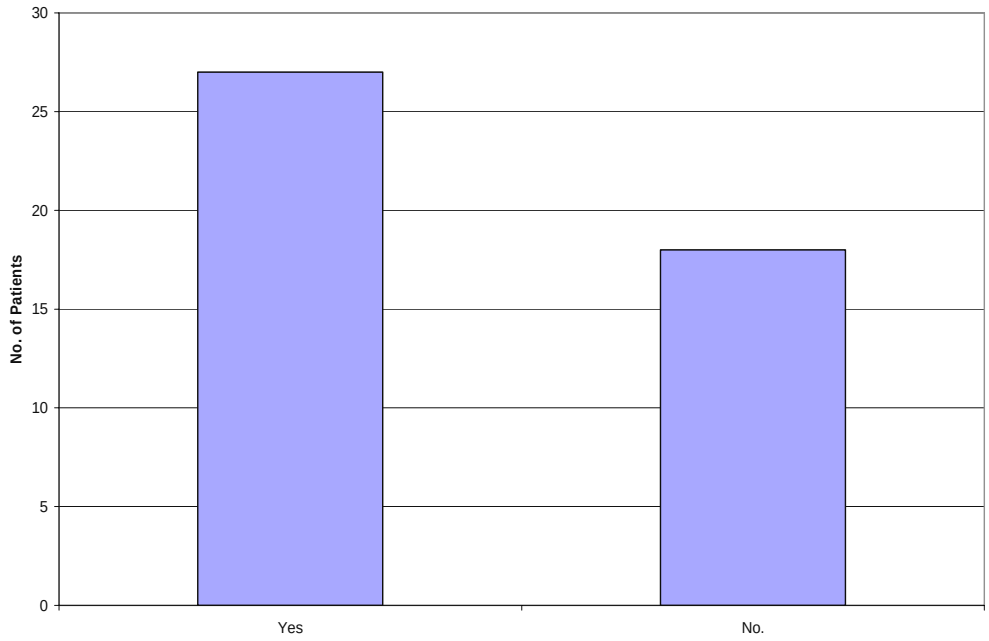
ECHO FINDINGS



ECG Findings



Cardiovascular Involvement



DISCUSSION

In the study group of 45 patients, 18 patients had no manifestations of cardiovascular system.

27 patients (i.e.,) 60% of patients in the study group had one or more of the cardiovascular manifestations. Cardiovascular involvement has been reported in 52 to 89% of patients in study by **Brigden W et al** (2) and by **Shearn M. A (5)**

Pericarditis

In the study, 12 patients had evidence of pericarditis proven by ECHO. They had mild to moderate pericardial effusion. This accounted for 27% of total cases. Pericarditis has been reported to be the most common manifestation of SLE with a prevalence of 6 to 45 % in various studies by **Godeau et al**. (8). **Rothfield et al (9)** and **Siegel(10)** found the prevalence to be around 25% in their studies.

Of these two had evidence of polyserositis in the form of pleural effusion and/or ascites. In one patient it was a part of pancarditis. None of the patients had frank renal failure, since it was carefully avoided to prevent confusion regarding the etiology of pericarditis.

Five of our patients had chest pain that could be attributed to pericarditis. Four patients had pericardial rub on auscultation. So less than 40% of patients had clinical evidence of pericarditis and majority were asymptomatic.

There were no cases of tamponade or constrictive pericarditis in the study group. Both of them are rare as reported by **Estes and Christian(11).**

Myocarditis

In the study group, 4 patients had myocardial dysfunction; approximately 9% of the group. 2 patients had global hypokinesia and 1 patient had regional hypokinesia of anterior wall. The fourth patient was a hypertensive and had grade I diastolic dysfunction.

Several studies have shown that primary myocardial involvement is uncommon. Studies by ***Dubois(22)***, ***Borenstein et al. (24)*** have shown the prevalence of myocarditis between 8 to 14%.

Winslow et al. (29) concluded that primary myocardial involvement in SLE is not commonly associated with significant clinical changes in left ventricular size and function and other pathogenic factors like hypertension and atherosclerosis are more important.

In this group, one patient's (patient no.13) first manifestation of the disease was cardiac failure, ECHO demonstrating global hypokinesia and EF of 43%. The patients symptoms and cardiac function markedly improved, when steroids were added to anti-failure medications.

Another patient (patient no.14), a 29 year old female was evaluated for pulmonary hypertension in the department of cardiology. She was referred to the department of medicine for the evaluation of generalized lymphadenopathy. On evalution,

she was positive for ANA, ds DNA. The excision biopsy of the node revealed Non-Hodgkins' Lymphoma. So this was a suspected case of primary pulmonary hypertension which later turned out to be a case of SLE with lymphoma.

All the patients with myocardial dysfunction were symptomatic and had exertional dyspnea. All the patients had pulmonary congestion and 3 had evidence of systemic venous congestion.

Endocarditis and Valvular lesions

The classical 'Libman-Sacks' endocarditis was not seen in any of the 45 patients.

In fact one patient was referred to the Intensive medical care unit of our hospital with florid SLE and she was found to have lesions suggestive of Libman-Sacks endocarditis in the echo done by the referring physician. Since she had a rapid downhill course, we could not include her in the study.

Mitral valve prolapse with or without MR was the most common valvular abnormality in the study. 11 patients had MVP which accounted for 24% of the study group.

Mitral regurgitatation, either associated with MVP or due to dilated LV was seen in 8 patients.

Mild AR was seen in 2 patients.

AR has been the common lesion reported by **Doherty** and **Seigel (10).** In patients on chronic steroid therapy mitral valve was more commonly involved. Along with this, the high prevalence of MVP in the general population could have accounted for the high prevalence of MVP and MR in this study.

One patient had TVP with TR. The overall incidence of valvular abnormalities is nearly 30% (14 cases).

Various studies by **Nihoyannopoulos et al (40**) have shown valvular involvement is common in SLE and it correleates with anti-cardiolipin antibodies.

Hypertension

Hypertension as defined by JNC VII, SBP >= 140 and or DBP >=90mmHg was seen in 6 patients. (i.e,) 15% of the patients in the study group. Most of these patients were chronic SLE patients on longterm steroid therapy, which could be the possible cause. One patient had concomitant renal failure. Two cases had evidence of LVH by ECHO.

Dubois (22) study found the prevalence of hypertension to be 25%. Hypertension in SLE is related to the development of nephropathy and to the use of systemic corticosteroids.

ECG abnormalities

20 patients had ECG abnormalities of which sinus tachycardia was most common; seen in one-third of patients. Apart from being associated with fever, anemia, overt myocardial dysfunction, isolated persistent tachycardia could bean early manifestation of myocarditis.

Inverted T-waves in Inferior leads, consistent with MVP in ECHO was seen in 2 out of 11 cases of MVP.

LVH (by voltage criteria) was seen in 2 cases.

Low voltage QRS complexes was seen in 1 case of moderate pericardial effusion.

Diffuse ST-T changes consistent with pericarditis was seen in 1 patient, though sinus tachycardia was more frequently present in these patients.

Poor progression of 'R' wave was seen in 1 patient, consistent with hypokinesia of anterior wall in ECHO.

One case had incomplete RBBB.

The overall performance of ECG abnormalities in the study group is 45%. In a study by **Dubois**, it was 34% and 74% in a study by ***Badui et al***.

CONCLUSION

The study showed cardiovascular involvement in SLE was 60% (27 patients.) Of these, 55% (15 patients) had symptoms that could be attributed to the cardiovascular system. Nearly another half were asymptomatic.

In the study, valvular abnormalities was the most common manifestation seen in nearly 30% (14 patients). Mitral valve prolapse with or without mitral regurgitation was the predominant lesion seen in 11 patients. Two patients had trivial aortic regurgitation and one had tricuspid valve prolapse with tricuspid regurgitation.

Pericarditis was the next common finding documented in 27% (12 cases), of which the majority were asymptomatic.

Hypertension was seen in 15% of patients and most of them were chronic SLE patients on longterm steroid therapy. Myocardial dysfunction was seen in less than 10% of the group.

Thus cardiovascular involvement in SLE is common and causes significant morbidity. Thorough evaluation of the cardiovascular system is essential for treating a case of SLE since it may be masked by other symptoms or the cardiac symptoms may be erroneously attributed to disease activity in other systems like pulmonary, renal and hematological.

Since valvular lesions are common in SLE, it is prudent to follow prophylaxis for infective endocarditis before dental or urological procedures.

In a case of suspected SLE detection of silent pericarditis, in the absence of serositis in other sites, helps in the diagnosis of SLE using the criteria.

PROFORMA

CARDIAC MANIFESTATIONS IN SLE

NAME AGE SEX

DIAGNOSED SLE IN :

CLINICAL FEATURES :

SYSTEMIC	-	FEVER FATIGUE ANOREXIA WEIGHT LOSS MALAISE
CUTANEOUS	-	PHOTOSENSITIVITY MALAR RASH ORAL ULCERS ALOPECIA DISCOID RASH
NEUROLOGICAL	-	HEADACHE SEIZURES MOOD / COGNITIVE DISTURBANCE MONO / POLYNEUROPATHY TIA / STROKE
MUSCULOSKELETAL	-	ARTHRALGIA MYALGIA HAND DEFORMITY
RENAL	-	OLIGURIA PEDAL EDEMA
THROMBOSIS	-	ARTERIAL VENOUS
RESPIRATORY	-	PLEURISY COUGH DYSPNEA
OCULAR	-	REDNESS DRY EYES

RELEVANT HISTORY :

SMOKING / ALCHOLIC
DM / HT / BA / PT

ABORTIONS

CURRENTLY ON (Rx) :

CLINICAL EXAMINATION :

PALLOR
RASH
LYMPHADENOPATHY
CLUBBING
PEDAL EDEMA
PERIORBITAL PUFFINESS
ORAL CAVITY

CARDIAC EVALUATION IN DETAIL

SYMPTOMS	SIGNS
CHEST PAIN	PULSE
DYSPNEA	BP
PALPITATION	JVP
SYNCOPE	S1 S2 P2
PEDAL EDEMA	ADDED SOUNDS

ECG

CXR HRCT

ECHO

OTHER LAB INVESTIGATIONS

HEMOGRAM / PS	BIOCHEMISTRY	URINALYSIS
Hb	UREA	
PCV	SUGAR	
TC	CREATININE	
DC	Na / K	
ESR	LIPID PROFILE	
PLATELETS		

BLOOD CULTURE

USG ABDOMEN

IMMUNOLOGY

ANA

dsDNA

CRP

aCL / LAC

OTHER INVESTIGATIONS

SYSTEMS INVOLVED IN THIS PATIENT/ CRITERIA FOR DIAGNOSIS:

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MASTER CHART

Sl. No	Name	Age (in Yrs)	Sex	Duration of SLE (in yrs)	CARDIA		
					Symptoms	Signs	EC
1	Ferozkhan	14	M	3/12	Nil	Tachycardia	Sin tachyc
2	Bharathi	27	F	2	Nil	Nil	WN
3	Jeevitha	15	F	1	Dyspnea	JVP+ Tachycardia	Sinus tachyc Incom RBBB
4	Subathra	22	F	3	Nil	Nil	WN
5	Sundari	36	F	16	Nil	Nil	WN
6	Selvi	21	F	3	Nil	Nil	WN
7	Sankari	22	F	3	Nil	Nil	WN
8	Ramesh	33	M	1	Dypnea palpitation	Tachycardia	Sin tachyc
9	Rekha	17	F	2	Palpitation	Midsystolic click – apex ESM+	WN
10	Sarasu	23	F	10/12	Chestpain	Pericardial rub	Sin tachyc
11	Salma	22	F	6/12	Chest pain	Pericardial rub	Low voltage Sinus tachyc
12	Sumathi	23	F	3/12	Nil	Nil	Sin tachyc
13	Valarmathy	20	F	3/12	Dyspnea palpitation & pedal edema	JVP+ bibasal rales	Sin tachyc
14	Elavarasi	29	F	2	Dyspnea palpitation & pedal edema	JVP+ Loud P2 bibasal rales	Sin tachyc

15	Dhanalakshmi	23	F	3/12	Chest pain	Pericardial rub	Sin tachyc
16	Satya	18	F	1	Nil	Nil	WN
17	Ramya	25	F	3	Nil	Nil	WN
18	Uma	34	F	7	Dyspnea	BP-160/100 bibasal rales	LV
19	Padma	37	F	10	Nil	BP-156/100	WN
20	Muthulakshmi	23	F	3/12	Nil	Nil	Sin tachyc
21	Jeya	40	F	10	Dyspnea palpitation	BP-152/90	LV
22	Durga	15	F	3/12	Nil	Nil	WN
23	Bhuvana	27	F	4	Nil	BP-140/90	WN
24	Kalaiselvi	14	F	2/12	Nil	Nil	WN
25	Mala	34	F	4	Nil	Nil	Sin tachyc
26	Rajeswari	32	F	1	Nil	Nil	WN
27	Selvi	32	F	12	Dysnea pedal edema	JVP+ LVS3+ bibasal rales	Sin tachyc PRWP V4
28	Kannamma	39	F	9	Nil	BP-150/100	WN
29	Kalamani	23	F	6/12	Nil	Nil	WN
30	Mary	28	F	2	Nil	Nil	T inve in infe lea
31	Hemalatha	30	F	5	Palpitation	ESM+ Apex	WN
32	Gayathri	32	F	3	Nil	Nil	WN
33	Sridevi	21	F	1	Nil	Nil	WN
34	Parameswari	34	F	2	Nil	Nil	T inv inf.le
35	Gomathy	30	F	3/12	Nil	Nil	WN
36	Shantha	27	F	3	Dyspnea	BP-150/70	Sin tachyc
37	Kannan	15	M	1	Nil	Nil	WN
38	Selvalakshmi	30	F	3	Chestpain palpitation	Pericardial rub	Sin tachyc

							Diffuse T chai
39	Neelammal	34	F	6	Nil	Nil	WN
40	Satyammal	20	F	2	Nil	Nil	WN
41	Muthammal	23	F	5	Chestpain	Ejection click+	Sinu tachyc
42	Aswini	19	F	4/12	Nil	Nil	WN
43	Manimegalai	25	F	2	Nil	Nil	WN
44	Arun	14	M	3/12	Nil	Nil	WN
45	Muthu	21	F	1	Nil	Nil	Sinu tachyc